

Amendments to the Specification

Please replace the paragraph at page 9, lines 18-23 with the following amended paragraph:

~~Figure 7 shows Figures 7A-7E show~~ the CTL responses against influenza NP in different mouse strains. Mice of different strains were immunised twice two weeks apart with a DNA vaccine V1J-NP encoding for the influenza nucleoprotein (open circles) or primed with the same DNA vaccine and two weeks later boosted with recombinant MVA expressing influenza virus nucleoprotein (closed circles). The CTL activity was determined in a standard ^{51}Cr -release assay with MHC class I-matched target cells.

Please replace the paragraph at page 11, lines 10-13 with the following amended paragraph:

~~Figure 15 shows Figures 15A-15C show~~ detection of SIV-specific MHC class I-restricted CD8+ T cells using tetramers. Each bar represents the percentage of CD8+ T cells specific for the Mamu-A*01/gag epitope at the indicated time point. One percent of CD8 T cells corresponds to about 5000/10⁶ peripheral blood lymphocytes.

Please replace the paragraph at page 11, lines 14-19 with the following amended paragraph:

~~Figure 16 shows Figures 16A-16C show~~ CTL induction in macaques following DNA/MVA immunisation. PBMC from three different macaques (CYD, DI and DORIS) were isolated at week 18, 19 and 23 and were restimulated with peptide CTPYDINQM [SEQ ID NO: 54] *in vitro*. After two restimulations with peptide CTPYDINQM [SEQ ID NO: 54] the cultures were tested for their lytic activity on peptide-pulsed autologous target cells.

Please replace the paragraph at page 36, lines 15-28, and continuing on page 37, lines 1-2 with the following amended paragraph:

CTL Induction to the Same Antigen in Different Mouse Strains

To address the question whether the boosting effect described above in BALB/c mice with two CTL epitopes SYIPSAEKI [SEQ ID NO: 67] derived from *P. berghei* CSP and RGPGRAFVTI [SEQ ID NO: 68] derived from HIV is a universal phenomenon, two sets of experiments were carried out. CTL responses to the influenza nucleoprotein were studied in five inbred mouse strains. In a first experiment three published murine CTL epitopes derived from the

influenza nucleoprotein were studied (see Table 3). Mice of three different H-2 haplotypes, BALB/c and DBA/2 (H-2^d), C57BL/6 and 129 (H-2^b); CBA/J (H-2^k), were used. One set of animals was immunised twice at two week intervals with the plasmid V1J-NP encoding the influenza nucleoprotein. Another set of identical animals was primed with V1J-NP and two weeks later boosted intravenously with 10⁶ ffu of MVA.NP, expressing influenza virus NP. The levels of CTL in individual mice were determined in a ⁵¹Cr-release assay with peptide restimulated splenocytes. As shown in ~~Figure 7~~ Figures 7A-7E, the DNA priming/MVA boosting immunisation regimen induced higher levels of lysis in all the mouse strains analysed and is superior to two DNA injections.

Please replace the paragraph at page 37, lines 3-10 with the following amended paragraph:

~~Figure 7 shows~~ Figures 7A-7E show the CTL responses against influenza NP in different mouse strains. Mice of different strains were immunised twice two weeks apart with a DNA vaccine V1J-NP encoding for the influenza nucleoprotein (open circles) or primed with the same DNA vaccine and two weeks later boosted with recombinant MVA expressing influenza virus nucleoprotein (closed circles). Two weeks after the last immunisation splenocytes were restimulated in vitro with the respective peptides (Table 3). The CTL activity was determined in a standard ⁵¹Cr-release assay with MHC class I-matched target cells.

Please replace the paragraph at page 54, lines 14-20 with the following amended paragraph:

Following two gene gun immunisations very low levels of CTL were detected using tetramer staining (~~Figure 15~~) Figures 15A-15C. Two weeks after the first MVA boosting, all three animals developed peptide specific CTL as detected by tetramer staining (~~Figure 15~~) Figures 15A-15C. This was reflected by the detection of moderate CTL responses following *in vitro* restimulation (~~Figure 16, week 19~~) (Figure 16B, week 19). The second boost with MVA.H induced very high levels of CD8+, antigen specific T cells (~~Figure 15~~) Figures 15A-15C and also very high levels of peptide specific cytotoxic T cells (~~Figure 16, week 23~~) (Figure 16C, week 23).

Please replace the paragraph at page 54, lines 21-29 with the following amended paragraph:

~~Figure 15 shows Figures 15A-15C show~~ detection of SIV-specific MHC class I-restricted CD8+ T cells using tetramers. Three Mamu-A*A01-positive macaques were immunised with plasmid DNA (gene gun) followed by MVA boosting as indicated. Frequencies of Mamu-A*A01/CD8 double-positive T cells were identified following FACS analysis. Each bar represents the percentage of CD8+ T cells specific for the Mamu-A*01/gag epitope at the indicated time point. One percent of CD8 T cells corresponds to about 5000/10⁶ peripheral blood lymphocytes. Thus the levels of epitope-specific CD8 T cells in the peripheral blood of these macaques are at least as high as the levels ~~observed~~ observed in the spleens of immunised and protected mice in the malaria studies.

Please replace the paragraph at page 55, lines 1-6 with the following amended paragraph:

~~Figure 16 shows Figures 16A-16C show~~ CTL induction in macaques following DNA/MVA immunisation. PBMC from three different macaques (CYD, DI and DORIS) were isolated at week 18, 19 and 23 and were restimulated with peptide CTPYDINQM [SEQ ID NO: 54] *in vitro*. After two restimulations with peptide CTPYDINQM [SEQ ID NO: 54] the cultures were tested for their lytic activity on peptide-pulsed autologous target cells. Strong CTL activity was observed.